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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/664,827	09/19/2000	Glen H. Erikson	E1047/20044	4947

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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 12/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No. 09/664,827	Applicant(s) ERIKSON ET AL.	
	Examiner Suryaprabha Chunduru	Art Unit 1637	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 02 October 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: *none*.

   Claim(s) objected to: *none*.

   Claim(s) rejected: *1-25,50 and 51*.

   Claim(s) withdrawn from consideration: *26-49 and 52*.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☒ Other: *See Continuation Sheet*

JEFFREY FREDMAN
PRIMARY EXAMINER

Continuation of 5. does NOT place the application in condition for allowance because: see attachement.

Continuation of 10. Other: Declaration submitted by the applicants is fully considered but further evidence is required to show the actual formation of W-C base pairing involving more than two strands in a multiplex structure as claimed.

Response to the request of reconsideration and declaration

1. Applicants' request for reconsideration and declaration are fully considered and found not persuasive because of the following reseasons:

Applicants' arguments regarding the rejection under 35 U.S.C. 112, first paragraph, are fully considered and found not persuasive. Applicants correctly pointed out M.P.E.P. 2164.01 citation that the invention is patentably enabled if one of ordinary skill in the art could make or use the invention from the disclosure in the patent application coupled with information known in the art without undue experimentation, however,the information teach Watson-Crick base pairing (W-C base pairing) between two DNA strands and no evidence is currently found in literature that Watson-Crick base pairing occurs involving more than two strands of DNA simultaneously. As discussed in the final office action the W-C bonding as in Fig. 1.7, given below:

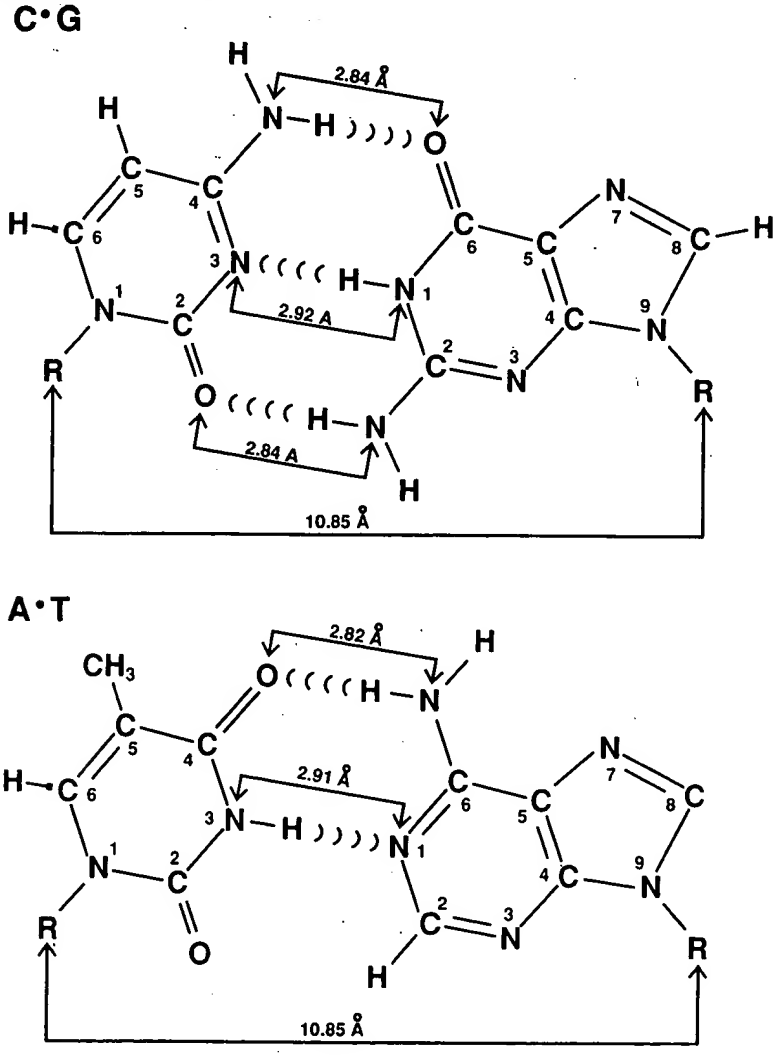

Figure 1.7 Watson–Crick base pairs. The interatom hydrogen bond distances and distances between the C1′ positions of the ribose sugars are indicated. The curved lines represent the hydrogen bonds. The curves are in the direction of the hydrogen bond acceptor (N or O atoms). Figure modified with permission from Arnott *et al.* (1965)

the three hydrogen bonds in G.C pair are shared between (i) amine group of cytosine with carboxyl group of guanine, (ii) amine group of cytosine with amine group of guanine (iii) carboxyl group of cytocine with amine group of guanine. There is no other hydrogen atom(s) to share to form a W-C base pairing with other purine or pyrimindine of a third or fourth strand as claimed in the instant invention. This limits the scope of the invention because the reverse pairing that is a hoogsteen base pairing occurs when such a situation occurs where more than two strands are involved in pairing with complementary nucleotides as discussed in the final office action.

Applicants' argue that the working examples shown in the instant patent application are ignored by the examiner, which is found not persuasive because the working examples shown in the disclosure do not provide any x-ray crystallographic or space-filling model as evidence to the Watson-Crick base pairing involving more than two strands in a multiplex structure. All the working examples and the cited U.S. patents do not support the actual W-C base pairing involving more than two strands.

Applicant's argument regarding the NMR studies in the particular reference cited by the Applicants, Zhang et al supporting the major groove-aligned G.C.G.C. and A.T.A.T. tetrads is fully considered. The issue here is that the tetrads formed in the reference involves two DNA strands at any given time, but not more than two strands participating in W-C base pairing simultaneously (see Fig.1, page 1074). The reference teaches the W-C base pairing in dimeric situation but not when three or four strands are involved in W-C pairing. The structure in the reference supports W-C paring between any two strands at any given time and do not support W-C pairing involving more than two strands simultaneously.

The declaration states that the W-C base pairing in the context of invention refers to specific association between opposing pairs of nucleic bases and may be referred to as a hybridization event, Further, the example 1 of the instant specification recites " quadruplex formation occurred on the basis of W-C base pair affinities, with a measurable and significantly greater amount of quardruplex formation between fully complementary homologous duplex strands" (see page 20, lines 13-16), which indicates that W-C base pairing occurs between two strands but not involving more than two strands simultaneously as claimed. conventional understanding does not support the actual W-C base pairing involving more that two strands. One of the ordinary skill in the art would not be convinced by the unpredictable art, where the basic biochemistry text book supports the thermodynamic unstability of the triplex structure as stated in the final office action.

Applicants' arguments and the declaration provided, did not substantiallly over come the rejection under 35 U.S.C. 112 first paragraph, enablement. X-ray crystalographic or space filling model evidence supporting W-C base paring involving more than two strands would over come the rejection. The rejection under 35 U.S.C. 101 is based on the rejection under 35 U.S.C. 112, first paragraph, enablement. It will be maintained since Applicants did not overcome the rejection under 35 U.S.C. 112, first paragraph.